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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,977	10/04/2005	David Deperthes	KZY-002USRCE	3931

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EXAMINER	
GUSSOW, ANNE	
ART UNIT	PAPER NUMBER
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,977	DEPERTHES ET AL.	
	Examiner	Art Unit	
	ANNE M. GUSSOW	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,8-10,12,17,28-30,43-46,49,50,53-60 and 63-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,8-10,12,17,28-30,43-46,49,50,53-60 and 63-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *sequence alignment*.

DETAILED ACTION

1. Claims 1, 28-30, 43, 44, 49, 57, 59, and 67 have been amended.

Claims 2, 3, 5-7, 11, 13-16, 18-27, 31-42, 47, 48, 51, 52, 61, and 62 have been cancelled.

2. Claims 1, 4, 8-10, 12, 17, 28-30, 43-46, 49, 50, 53-60, and 63-68 are under examination.

3. The following office action contains NEW GROUNDS of Rejection.

Rejections Withdrawn

4. The rejection of claim 49 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn in view of applicant's amendment to the claim.

5. The rejection of claims 1, 4, 6-10, 12, 17, 28-30, 41-46, and 49-68 under 35 U.S.C. 112, first paragraph as lacking enablement is withdrawn in view of applicant's amendment to the claims.

Claim Objections

6. Claim 1 is objected to because of the following informalities: The "and/or" language in line 2 is not a proper Markush group. A proper Markush group recites the

language "selected from the group consisting of ... and ..." Appropriate correction is required.

NEW GROUNDS of Rejection

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1, 4, 8-10, 12, 17, 43-46, 49, 50, 53-60, and 63-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Houimel, et al. (International Journal of Cancer, 2001. Vol. 92, pages 748-755, as cited in the office action mailed October 13, 2006) in view of Wickham, et al. (US PG PUB 2003/0099619, filed November 25, 2002), Koh, (US PAT 7,081,443, filed October 18, 2002) and Rusch, et al. (Cytokine and Growth Factor Reviews, 1996. Vol. 7, pages 133-141) and Todaro, et al. (EP 0190018, published August 6, 1986).

The claims recite a recombinant fusion peptabody, which binds to an epidermal growth factor receptor selected from the group consisting of ErbB-1, ErbB-3, and/or ErbB-4, comprising: (a) a cartilage oligomer matrix polypeptide comprising amino acid residues 16 to 64 of SEQ ID NO: 2 (b) a peptide enhancer sequence having an amino acid sequence selected from the group consisting of YSFE (SEQ ID NO: 5), YSFEDL (SEQ ID NO: 6), and YSFEDLYRR (SEQ ID NO: 9) and located at the N terminus of the peptabody; (c) a hinge region of an immunoglobulin polypeptide comprising amino acid residues 65 to 83 of SEQ ID NO:2, located at the C terminus of the cartilage oligomer matrix polypeptide portion; and (d) an epidermal growth factor receptor ligand selected from the group consisting of any of SEQ ID NOs: 10-29, which can bind to the epidermal growth factor receptor, located at the C terminus of the hinge region, wherein said recombinant fusion peptabody is capable of inducing cellular death in a

cell expressing said epidermal growth factor receptor, wherein said recombinant fusion peptabody is multimeric, further comprising a polyhistidine tag sequence, further comprising at least one effector region, wherein the effector region comprises a cytotoxin or a detection moiety, wherein said detection moiety is fluorescent. A pharmaceutical composition comprising the recombinant fusion peptabody of claim 1, and a pharmaceutically acceptable carrier.

Houimel, et al. teach a recombinant peptabody that binds to ErbB2 comprising a human cartilage oligomeric matrix protein (COMP) identical to residues 16 to 64 of SEQ ID No. 2 (page 749 2nd column 1st full paragraph), a hinge region derived from human IgA1 identical to residues 65 to 83 of SEQ ID No. 2 (page 749 2nd column 1st full paragraph) and a polyhistidine tag sequence (figure 2). Houimel, et al. teach targeting of breast cancer cells with the peptabody (figure 5). Houimel, et al. do not teach the enhancer sequences of SEQ ID Nos. 5, 6, or 9 or the ligand sequences of SEQ ID Nos. 10-29. Houimel, et al. do not teach the peptabody fused to a fluorescent tag or in a pharmaceutical composition. These deficiencies are made up for in the teachings of Wickham, et al., Koh, and Todaro, et al.

Wickham, et al. teach a peptide (SEQ ID No. 21) which is identical to the instant SEQ ID No. 9 in an adenoviral construct for binding the virus to an integrin receptor on a cell. Wickham, et al. teach that the integrin receptors are upregulated in tumor tissue (paragraph 17).

Koh teaches a multimeric fusion molecule including a COMP domain and a ligand including EGF (column 4). Koh teaches the fusion molecules labeled with a

detectable label including a fluorescent tag (column 8 lines 55-60). Koh teaches the fusion molecules in a pharmaceutical composition (column 15 lines 48-57).

Rusch, et al. teach that TGF alpha is an EGFR ligand.

Todaro, et al. teach the peptide sequence of SEQ ID No. 25 of a TGF alpha protein (see sequence alignment).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced a peptabody comprising the cartilage oligomer matrix polypeptide (COMP), hinge and peptabody structure of Houimel, et al. with the peptide sequence of Wickham, et al., the fluorescent tag of Koh, and the ligand sequence of Todaro, et al. for diagnosing or treating breast cancer.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced a peptabody comprising the cartilage oligomer matrix polypeptide (COMP), hinge and peptabody structure of Houimel, et al. with the peptide sequence of Wickham, et al., the fluorescent tag of Koh, and the ligand sequence of Todaro, et al. for diagnosing or treating breast cancer because Wickham, et al. teach the integrin binding peptide binds a cellular receptor and thus brings the viral construct in close proximity to the cell for internalization (see abstract and paragraphs 16-17). Additionally, Houimel, et al. teach different ligand sequences that bind to ErbB2 (table 1); therefore, one of ordinary skill in the art would be motivated to and have a reasonable expectation of success to replace the ligand of Houimel, et al. with other ligand sequences, such as the peptide sequence of Todaro, et al., known to target the EGFR according to Rusch, et al. Thus, it would have been

obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the structure of Houimel, et al and produce a fusion peptabody comprising the peptides in view of Wickham, et al., Koh, Rusch, et al. and Todaro, et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

11. Claims 1, 4, 8-10, 12, 17, 28-30, 43-46, 49, 50, 53-60, and 63-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Houimel, et al. (International Journal of Cancer, 2001. Vol. 92, pages 748-755, as cited in the office action mailed October 13, 2006) in view of Wickham, et al. (US PG PUB 2003/0099619, filed November 25, 2002), Koh, (US PAT 7,081,443, filed October 18, 2002) and Rusch, et al. (Cytokine and Growth Factor Reviews, 1996. Vol. 7, pages 133-141) and Todaro, et al. (EP 0190018, published August 6, 1986) as applied to claims 1, 4, 8-10, 12, 17, 43-46, 49, 50, 53-60, and 63-68 above and further in view of Rosen, et al. (US PAT 6,926,898, filed April 12, 2001).

Claims 1, 4, 8-10, 12, 17, 43-46, 49, 50, 53-60, and 63-68 have been described supra. Claims 28-30 recite a kit for treating cancer characterized by expression of an epidermal growth factor receptor selected from the group consisting of ErbB 1, ErbB3, and ErbB4, in a human patient, said kit comprising the recombinant fusion peptabody of claim 1 and/or instructions for administering the recombinant fusion peptabody to the human patient for the treatment of cancer, further comprising a separate pharmaceutical dosage form comprising an additional anti-cancer agent selected from the group

consisting of a chemotherapeutic agent, an anti-epidermal growth factor receptor antibody, a radioimmunotherapeutic agent, and combinations thereof. A kit for diagnosing cancer characterized by expression of an epidermal growth factor receptor selected from the group consisting of ErbB 1, ErbB3, and ErbB4, in a human patient, said kit comprising the recombinant fusion peptabody of claim 10, and instructions for use.

Houimel, et al. has been described supra. Houimel, et al. do not teach the enhancer sequences of SEQ ID Nos. 5, 6, or 9 or the ligand sequences of SEQ ID Nos. 10-29. Houimel, et al. do not teach the peptabody fused to a fluorescent tag or in a pharmaceutical composition. Houimel, et al. do not teach the peptabody in a kit. These deficiencies are made up for in the teachings of Wickham, et al., Koh, Todaro, et al., and Rosen, et al.

Wickham, et al. has been described supra.

Koh has been described supra.

Rusch, et al. has been described supra.

Todaro, et al. has been described supra.

Rosen, et al. teach pharmaceutical formulations of fusion proteins in a kit for the treatment or detection of cancer (column 2 lines 43-46). Rosen, et al. teach the kit may contain instructions (column 2 lines 46-48). Rosen, et al. teach the fusion proteins may be conjugated to a diagnostic or therapeutic agent including fluorescent materials (column 100 lines 47-65). Rosen, et al. teach the fusion proteins may be administered

alone or in combination with other therapeutic agents including chemotherapeutic agents (column 148 lines 20-38).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced a peptabody comprising the cartilage oligomer matrix polypeptide (COMP), hinge and peptabody structure of Houimel, et al. with the peptide sequence of Wickham, et al., the fluorescent tag of Koh, and the ligand sequence of Todaro, et al. in a kit as taught by Rosen, et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced a peptabody comprising the cartilage oligomer matrix polypeptide (COMP), hinge and peptabody structure of Houimel, et al. with the peptide sequence of Wickham, et al., the fluorescent tag of Koh, and the ligand sequence of Todaro, et al. in a kit of Rosen, et al. because Rosen, et al. teach reagents including antibodies in a kit for the detection and treatment of cancer (column 2 lines 43-46) and Wickham, et al. teach that the integrin binding peptide binds a cellular receptor and thus brings the viral construct in close proximity to the cell for internalization (see abstract and paragraphs 16-17). Additionally, Houimel, et al. teach different ligand sequences that bind to ErbB2 (table 1); therefore, one of ordinary skill in the art would be motivated to and have a reasonable expectation of success to replace the ligand of Houimel, et al. with other ligand sequences, such as the peptide sequence of Todaro, et al. The instructions for use included in a kit or article manufacture constitute an "intended use" for that kit or article of manufacture. Intended use does not impart patentable weight to a product (see MPEP 2111.03).

Thus, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the structure of Houimel, et al and produce a fusion peptabody comprising the peptides of Wickham, et al., Koh, and Todaro, et al. in a kit in view of Rosen, et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

12. No claims are allowed.

13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Chino and Hayakawa (EP498222A1, published August 12, 1992.). Chino and Hayakawa teach a peptide identical to SEQ ID No. 11, see sequence alignment.

Delaey, et al. (WO9723507, published July 3, 1997). Delaey, et al. teach a peptide identical to SEQ ID No. 26, see sequence alignment.

Sasada, et al. (WO9630506, published October 3, 1996). Sasada, et al. teach a peptide identical to SEQ ID No. 28, see sequence alignment.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNE M. GUSSOW whose telephone number is (571)272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

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Anne M. Gussow
July 1, 2009

/Anne M Gussow/
Examiner, Art Unit 1643

/David J Blanchard/
Primary Examiner, Art Unit 1643